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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/646,493 | 08/21/2003 | Eric Rose | 50634-BA | 9464 |

7590 07/18/2005

John P. White
Cooper & Dunham LLP
1185 Avenue of the Americas
New York, NY 10036

| EXAMINER | |
|---|---|
| RUSSEL, JEFFREY E | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1654 | |

DATE MAILED: 07/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/646,493 | ROSE ET AL. | |
| | Examiner | Art Unit | |
| | Jeffrey E. Russel | 1654 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *25 April 2005 and 03 June 2005*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *9 and 38-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *9 and 38-44* are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 June 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet*.

1. This application contains claims directed to the following patentably distinct species of the claimed invention:

(1) Pharmaceutical compositions comprising an inactive Christmas factor, classified in Class 514, Subclass 8.

(2) Pharmaceutical compositions comprising a carboxylated Christmas factor, classified in Class 514, Subclass 8.

(3) Pharmaceutical compositions comprising a des-γ-carboxyl Factor IX, classified in Class 424, Subclass 94.64.

(4) Pharmaceutical compositions comprising Factor IX lacking a calcium-dependent membrane binding function, classified in Class 424, Subclass 94.64.

(5) Pharmaceutical compositions comprising Factor IX Bm Kiryu, classified in Class 424, Subclass 94.64.

(6) Pharmaceutical compositions comprising glycosylated Factor IXa, classified in Class 424, Subclass 94.64.

(7) Pharmaceutical compositions comprising Factor IXa having β-hydroxylation of aspartic acid, classified in Class 424, Subclass 94.64.

(8) Pharmaceutical compositions comprising Factor IXa having γ-carboxylation of glutamic acid, classified in Class 424, Subclass 94.64.

(9) Pharmaceutical compositions comprising Factor IXa having propeptide cleavage, classified in Class 424, Subclass 94.64.

(10) Pharmaceutical compositions comprising an inactive mutein form of Factor IXa having a Ser185 to Ala substitution, classified in Class 424, Subclass 94.64.

(11) Pharmaceutical compositions comprising an inactive mutein form of Factor IXa including only residues 1-47, classified in Class 424, Subclass 94.64.

(12) Pharmaceutical compositions comprising an inactive mutein form of Factor IXa having a Val313 to Asp substitution in the catalytic domain of Factor IX, classified in Class 424, Subclass 94.64.

(13) Pharmaceutical compositions comprising an inactive mutein form of Factor IXa having a Gly311 to Glu substitution in the catalytic domain of Factor IX, classified in Class 424, Subclass 94.64.

(14) Pharmaceutical compositions comprising an inactive mutein form of Factor IXa having a Gly311 to Glu substitution in the catalytic domain of Factor IX, classified in Class 424, Subclass 94.64.

(15) Pharmaceutical compositions comprising an inactive mutein form of Factor IXa having a Gly311 to Arg318 deletion, classified in Class 424, Subclass 94.64.

(16) Pharmaceutical compositions comprising an inactive mutein form of Factor IXa having an amino acid substitution at His221, classified in Class 424, Subclass 94.64.

(17) Pharmaceutical compositions comprising an inactive mutein form of Factor IXa having an amino acid substitution at Asp269, classified in Class 424, Subclass 94.64.

(18) Pharmaceutical compositions comprising an inactive mutein form of Factor IXa having an amino acid substitution at Ser365, classified in Class 424, Subclass 94.64.

(19) Pharmaceutical compositions comprising an inactive mutein form of Factor IXa having an amino acid substitution at His41 in the heavy chain of Factor IXa, classified in Class 424, Subclass 94.64.

(20) Pharmaceutical compositions comprising an inactive mutein form of Factor IXa having an amino acid substitution at Asp89 in the heavy chain of Factor IXa, classified in Class 424, Subclass 94.64.

(21) Pharmaceutical compositions comprising an inactive mutein form of Factor IXa having an amino acid substitution at Ser185 in the heavy chain of Factor IXa, classified in Class 424, Subclass 146.1.

(22) Pharmaceutical compositions comprising an anti-Factor IX antibody or fragment thereof, classified in Class 424, Subclass 146.1.

(23) Pharmaceutical compositions comprising a small organic molecule, classified in Class 514, Subclass 1.

(24) Pharmaceutical compositions comprising a peptidomimetic, classified in Class 514, Subclass 1.

These species are materially distinct from one another because of their materially different structures. Note that there is no common structure among the Christmas factor/Factor IX/Factor IXa derivatives, the antibodies, the small organic molecules, and the peptidomimetics. No one structural feature is required for all of the recited Factor IXa compounds. Searching all of the claimed species would constitute an undue burden upon the examiner because each species will require divergent sequence and text searches, depending upon the elected invention.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 9, 43, and 44 are generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

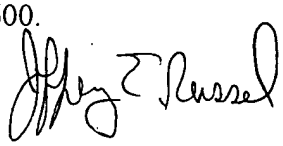
2. Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

3. The Sequence Listing submitted by Applicants on April 25, 2005 was not approved by STIC for the reasons set forth in the attached Raw Sequence Listing Error Report. Applicants may submit a corrected sequence listing now, or they can wait until the next action on the merits in which the examiner will formally require submission of a corrected sequence listing.

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (571) 272-0969. The examiner can normally be reached on Monday-Thursday from 8:30 A.M. to 6:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Bruce Campell can be reached at (571) 272-0974. The fax number for formal communications to be entered into the record is (571) 273-8300; for informal communications such as proposed amendments, the fax number (571) 273-0969 can be used. The telephone number for the Technology Center 1600 receptionist is (571) 272-1600.



Jeffrey E. Russel

Primary Patent Examiner

Art Unit 1654

JRussel

July 11, 2005

Continuation of Attachment(s) 6). Other: Raw Sequence Listing Error Report.

# STIC Biotechnology Systems Branch

# RAW SEQUENCE LISTING ERROR REPORT

**The Biotechnology Systems Branch of the Scientific and Technical Information Center (STIC) detected errors when processing the following computer readable form:**

Application Serial Number: 10/646,493
Source: IFW16
Date Processed by STIC: 4/29/05

**THE ATTACHED PRINTOUT EXPLAINS DETECTED ERRORS.**
**PLEASE FORWARD THIS INFORMATION TO THE APPLICANT BY EITHER:**
1) **INCLUDING A COPY OF THIS PRINTOUT IN YOUR NEXT COMMUNICATION TO THE APPLICANT, WITH A NOTICE TO COMPLY or,**
2) **TELEPHONING APPLICANT AND FAXING A COPY OF THIS PRINTOUT, WITH A NOTICE TO COMPLY**

**FOR CRF SUBMISSION AND PATENTIN SOFTWARE QUESTIONS, PLEASE CONTACT MARK SPENCER, TELEPHONE: 571-272-2510; FAX: 571-273-0221**

TO REDUCE ERRORED SEQUENCE LISTINGS, PLEASE USE THE CHECKER VERSION 4.2.2 PROGRAM, ACCESSIBLE THROUGH THE U.S. PATENT AND TRADEMARK OFFICE WEBSITE. SEE BELOW FOR ADDRESS:

**http://www.uspto.gov/web/offices/pac/checker/chkrnote.htm**

Applicants submitting genetic sequence information electronically on diskette or CD-Rom should be aware that there is a possibility that the disk/CD-Rom may have been affected by treatment given to all incoming mail.
Please consider using alternate methods of submission for the disk/CD-Rom or replacement disk/CD-Rom.
Any reply including a sequence listing in electronic form should NOT be sent to the 20231 zip code address for the United States Patent and Trademark Office, and instead should be sent via the following to the indicated addresses:

1. EFS-Bio (<http://www.uspto.gov/ebc/efs/downloads/documents.htm>, **EFS Submission User Manual** - ePAVE)
2. U.S. Postal Service: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450
3. Hand Carry, Federal Express, United Parcel Service, or other delivery service (EFFECTIVE 01/14/05): U.S. Patent and Trademark Office, Mail Stop Sequence, Customer Window, Randolph Building, 401 Dulany Street, Alexandria, VA 22314

Revised 01/24/05

## Raw Sequence Listing Error Summary

| ERROR DETECTED | SUGGESTED CORRECTION | SERIAL NUMBER: 10/646,493 |
|---|---|---|

ATTN: NEW RULES CASES: PLEASE DISREGARD ENGLISH "ALPHA" HEADERS, WHICH WERE INSERTED BY PTO SOFTWARE

| | | |
|---|---|---|
| 1 ✓ | Wrapped Nucleics<br>Wrapped Aminos | The number/text at the end of each line "wrapped" down to the next line. This may occur if your file was retrieved in a word processor after creating it. Please adjust your right margin to .3; this will prevent "wrapping." |
| 2 ____ | Invalid Line Length | The rules require that a line not exceed 72 characters in length. This includes white spaces. |
| 3 ____ | Misaligned Amino Numbering | The numbering under each 5th amino acid is misaligned. Do not use tab codes between numbers; use space characters, instead. |
| 4 ____ | Non-ASCII | The submitted file was not saved in ASCII(DOS) text, as required by the Sequence Rules. Please ensure your subsequent submission is saved in ASCII text. |
| 5 ____ | Variable Length | Sequence(s) ____ contain n's or Xaa's representing more than one residue. Per Sequence Rules, each n or Xaa can only represent a single residue. Please present the maximum number of each residue having variable length and indicate in the <220>-<223> section that some may be missing. |
| 6 ____ | PatentIn 2.0 "bug" | A "bug" in PatentIn version 2.0 has caused the <220>-<223> section to be missing from amino acid sequences(s) _____. Normally, PatentIn would automatically generate this section from the previously coded nucleic acid sequence. Please manually copy the relevant <220>-<223> section to the subsequent amino acid sequence. This applies to the mandatory <220>-<223> sections for Artificial or Unknown sequences. |
| 7 ____ | Skipped Sequences (OLD RULES) | Sequence(s) _____ missing. If intentional, please insert the following lines for each skipped sequence:<br>(2) INFORMATION FOR SEQ ID NO:X: (insert SEQ ID NO where "X" is shown)<br>(i) SEQUENCE CHARACTERISTICS: (Do not insert any subheadings under this heading)<br>(xi) SEQUENCE DESCRIPTION:SEQ ID NO:X: (insert SEQ ID NO where "X" is shown)<br>This sequence is intentionally skipped<br><br>Please also adjust the "(ii) NUMBER OF SEQUENCES:" response to include the skipped sequences. |
| 8 ____ | Skipped Sequences (NEW RULES) | Sequence(s) _____ missing. If intentional, please insert the following lines for each skipped sequence.<br><210> sequence id number<br><400> sequence id number<br>000 |
| 9 ____ | Use of n's or Xaa's (NEW RULES) | Use of n's and/or Xaa's have been detected in the Sequence Listing.<br>Per 1.823 of Sequence Rules, use of <220>-<223> is MANDATORY if n's or Xaa's are present.<br>In <220> to <223> section, please explain location of n or Xaa, and which residue n or Xaa represents. |
| 10 ____ | Invalid <213> Response | Per 1.823 of Sequence Rules, the only valid <213> responses are: Unknown, Artificial Sequence, or scientific name (Genus/species). <220>-<223> section is required when <213> response is Unknown or is Artificial Sequence |
| 11 ____ | Use of <220> | Sequence(s) _____ missing the <220> "Feature" and associated numeric identifiers and responses.<br>Use of <220> to <223> is MANDATORY if <213> "Organism" response is "Artificial Sequence" or "Unknown." Please explain source of genetic material in <220> to <223> section.<br>(See "Federal Register," 06/01/1998, Vol. 63, No. 104, pp. 29631-32) (Sec. 1.823 of Sequence Rules) |
| 12 ____ | PatentIn 2.0 "bug" | Please do not use "Copy to Disk" function of PatentIn version 2.0. This causes a corrupted file, resulting in missing mandatory numeric identifiers and responses (as indicated on raw sequence listing). Instead, please use "File Manager" or any other manual means to copy file to floppy disk. |
| 13 ____ | Misuse of n/Xaa | "n" can only represent a single nucleotide; "Xaa" can only represent a single amino acid |

IFW16

RAW SEQUENCE LISTING DATE: 04/29/2005
PATENT APPLICATION: US/10/646,493 TIME: 13:57:29

Input Set : A:\PTO.YF.txt
Output Set: N:\CRF4\04292005\J646493.raw

3 <110> APPLICANT: Rose, Eric
4 Stern, David
5 Schmidt, Ann Marie
6 Spanier, Talia
8 <120> TITLE OF INVENTION: METHOD FOR INHIBITING THROMBOSIS IN A PATIENT WHOSE BLOOD IS SUBJECTED TO
9 EXTRACORPOREAL CIRCULATION
11 <130> FILE REFERENCE: 50634-BA/JPW/AJM/AAB
13 <140> CURRENT APPLICATION NUMBER: 10/646,493
14 <141> CURRENT FILING DATE: 2003-08-21
16 <150> PRIOR APPLICATION NUMBER: US 09/053,872
17 <151> PRIOR FILING DATE: 1998-04-01
19 <150> PRIOR APPLICATION NUMBER: PCT/US97/08282
20 <151> PRIOR FILING DATE: 1997-05-15
22 <150> PRIOR APPLICATION NUMBER: US 08/648,561
23 <151> PRIOR FILING DATE: 1996-05-16
25 <160> NUMBER OF SEQ ID NOS: 3
27 <170> SOFTWARE: PatentIn version 3.1

Does Not Comply
Corrected Diskette Needed

pp 1, 3-5

ERRORED SEQUENCES

29 <210> SEQ ID NO: 1
30 <211> LENGTH: 29
31 <212> TYPE: DNA
32 <213> ORGANISM: Artificial
34 <220> FEATURE:
35 <221> NAME/KEY: misc_feature
36 <222> LOCATION: (14)..(16)
37 <223> OTHER INFORMATION: nnn is the complement to a DNA codon for any one of the standard
38 amino acids other than serine ← Serine
40 <220> FEATURE:
41 <221> NAME/KEY: misc_feature
42 <222> LOCATION: (1)..(29)
43 <223> OTHER INFORMATION: primer
45 <220> FEATURE:
46 <221> NAME/KEY: misc_feature
47 <222> LOCATION: (29)..(29)
48 <223> OTHER INFORMATION: v is c, ca, or caa
50 <220> FEATURE:
51 <221> NAME/KEY: misc_feature
52 <222> LOCATION: (1)..(1)
53 <223> OTHER INFORMATION: w is a

per Sequence Rules, "v" can only represent a single nucleotide: a or c or g

see p. 3

55 <220> FEATURE:

RAW SEQUENCE LISTING DATE: 04/29/2005
PATENT APPLICATION: US/10/646,493 TIME: 13:57:29

Input Set : A:\PTO.YF.txt
Output Set: N:\CRF4\04292005\J646493.raw

Per Sequence Rules, "w" can only represent a or t/u

56 <221> NAME/KEY: misc_feature
57 <222> LOCATION: (1)..(1)
58 <223> OTHER INFORMATION: w is t, gt, or agt
60 <400> SEQUENCE: 1
E--> 61 wacagttcct ctannncccc ctggggtav 29
62 29 (see item 1 on Error Summary Sheet)
65 <210> SEQ ID NO: 2
66 <211> LENGTH: 29
67 <212> TYPE: DNA
68 <213> ORGANISM: Artificial
70 <220> FEATURE:
71 <221> NAME/KEY: misc_feature
72 <222> LOCATION: (14)..(16)
73 <223> OTHER INFORMATION: nnn is the complement to a DNA codon for any one of the standard
74 amino acids other than aspartic acid and cysteine
76 <220> FEATURE:
77 <221> NAME/KEY: misc_feature
78 <222> LOCATION: (1)..(29)
79 <223> OTHER INFORMATION: primer
81 <220> FEATURE:
82 <221> NAME/KEY: misc_feature
83 <222> LOCATION: (29)..(29)
84 <223> OTHER INFORMATION: v is c, ct, ctt
"v" can only represent a or c or g
86 <220> FEATURE:
87 <221> NAME/KEY: misc_feature
88 <222> LOCATION: (1)..(1)
89 <223> OTHER INFORMATION: w is a, ta, or tta
"w" can only represent a or t/u
91 <400> SEQUENCE: 2
E--> 92 wttcatgtta gtannntaac gcgaagacv 29 (see item 1 on Error Summary Sheet)
93 29
96 <210> SEQ ID NO: 3
97 <211> LENGTH: 35
98 <212> TYPE: DNA
99 <213> ORGANISM: Artificial
101 <220> FEATURE:
102 <221> NAME/KEY: misc_feature
103 <222> LOCATION: (17)..(19)
104 <223> OTHER INFORMATION: nnn is the complement to a DNA codon for any one of the standard
105 amino acids other than histidine and cysteine.
107 <220> FEATURE:
108 <221> NAME/KEY: misc_feature
109 <222> LOCATION: (1)..(35)
110 <223> OTHER INFORMATION: Primer
112 <220> FEATURE:
113 <221> NAME/KEY: misc_feature
114 <222> LOCATION: (35)..(35)
115 <223> OTHER INFORMATION: v is c, cc, or cca
see above for valid representation of "v"
117 <220> FEATURE:
118 <221> NAME/KEY: misc_feature

RAW SEQUENCE LISTING DATE: 04/29/2005
PATENT APPLICATION: US/10/646,493 TIME: 13:57:29

Input Set : A:\PTO.YP.txt
Output Set: N:\CRF4\04292005\J646493.raw

119 <222> LOCATION: (1)..(1)
120 <223> OTHER INFORMATION: w is a, ta, or tta
122 <220> FEATURE:
123 <221> NAME/KEY: misc_feature
124 <222> LOCATION: (1)..(1)
125 <223> OTHER INFORMATION: w is a, aa, or taa
127 <400> SEQUENCE: 3
E--> 128 wttacattga cgacggnnna cacaactttg accav
129 35

(see p. 3 for valid representation of 'w')

35 (see item 7 on Error Summary Sheet)

RAW SEQUENCE LISTING ERROR SUMMARY DATE: 04/29/2005
PATENT APPLICATION: US/10/646,493 TIME: 13:57:30

Input Set : A:\PTO.YF.txt
Output Set: N:\CRF4\04292005\J646493.raw

Invalid Line Length:
The rules require that a line not exceed 72 characters in length. This includes spaces.

Seq#:1; Line(s) 8

Invalid <213> Response:
Use of "Artificial" only as "<213> Organism" response is incomplete,
per 1.823(b) of New Sequence Rules. Valid response is Artificial Sequence.

Seq#:1,2,3

VERIFICATION SUMMARY DATE: 04/29/2005
PATENT APPLICATION: US/10/646,493 TIME: 13:57:30

Input Set : A:\PTO.YF.txt
Output Set: N:\CRF4\04292005\J646493.raw

L:61 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:1 after pos.:0
L:61 M:254 E: No. of Bases conflict, LENGTH:Input:0 Counted:29 SEQ:1
L:92 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:2 after pos.:0
L:92 M:254 E: No. of Bases conflict, LENGTH:Input:0 Counted:29 SEQ:2
L:128 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:3 after pos.:0
L:128 M:254 E: No. of Bases conflict, LENGTH:Input:0 Counted:35 SEQ:3